

DCIEM 3L 2000-117

MILITARY PSYCHOLOGY, 2002, 14(1), 23-47

Effects of Modafinil on Cognitive Performance During 40 Hr of Sleep Deprivation in a Warm Environment

Joseph V. Baranski, Valerie Gil, Tom M. McLellan,
and Dianne Moroz

*Defence and Civil Institute of Environmental Medicine
Toronto, Canada*

Alain Buguet

*Centre de Recherches du Service de Santé des Armées
La Tronche Cédex, France*

Manny Radomski

*Defence and Civil Institute of Environmental Medicine
Toronto, Canada*

This study examined the effect of the psychostimulant modafinil on cognitive performance during 40 hr of sleep deprivation in a warm environment. Five men were randomly assigned to a modafinil (3×100 mg/24 hr) and a placebo trial on consecutive weeks, with a 5-day intervening "wash-out" period. Each trial involved a thermoneutral control day (outside of the climatic chamber) followed by a 40-hr sleep deprivation period in a climatic chamber at 30°C with 50% relative humidity. Ten cognitive testing sessions were conducted on each trial; each session lasted approximately 45 min, and they occurred at 6-hr intervals. The task battery included subjective assessments of mood, fatigue, and motivation and cognitive assessments of serial reaction time, logical reasoning (logical reasoning task [LRT]), visual comparison (CMP), mental addition (ADD), vigilance (detection of repeated numbers [DRN]), and multitasking. In addition, for 4 of the cognitive tasks that permitted a quantitative index of response accuracy (i.e., LRT, CMP, DRN, and ADD), participants provided estimates of their performance before and after each session to permit an evaluation

Requests for reprints should be sent to Joseph V. Baranski, Defence and Civil Institute of Environmental Medicine, 1133 Sheppard Avenue West, PO Box 2000, Toronto, Ontario, Canada M3M 3B9
E-mail: joe.baranski@dciem.dnd.ca

of the extent to which they could accurately self-monitor their own cognitive abilities. The findings revealed that (a) despite significant increases in core body temperature, cognitive performance was largely unaffected by the warm environment *per se*; (b) sleep loss induced a general reduction in cognitive performance that was largely but not completely eliminated by modafinil, and (c) participants were able to accurately self-monitor their own cognitive capabilities during both the placebo and modafinil trials. In this article, we discuss the potential utility of modafinil in sustained military operations and the general implications of these findings for Hancock's (1986) theory of sustained attention under thermal stress.

Military operations demand optimal performance under conditions that can approach the limits of human tolerance. For example, in recent conflicts such as the Gulf War and altercations in Somalia and Rwanda, military personnel were required to perform around-the-clock or sustained operations while under extreme thermal stress. Although technological advances have improved human performance, the chronic problem of fatigue due to sleep loss provides an example of where technology is limited and viable options are few. One alternative that historically has received considerable attention from the sleep-loss and performance research community is stimulant countermeasures (see Babkoff & Krueger, 1992).

MODAFINIL

Modafinil (diphenylmethyl-sulfinyl-2 acetamide) is a relatively new synthetic stimulant that has attracted considerable interest based on a growing body of evidence that suggests that the compound promotes vigilance and arousal without toxicity, tolerance, dependency, or significant sleep disturbances (Laborit & Lafon, 1994). Although the precise mechanism of action of modafinil is not fully understood, early animal studies suggest that modafinil acts centrally as an $\alpha 1$ -adrenergic agonist (Duteil, Rambert, Personnier, Gombert, & Assous, 1979; Duteil et al., 1990). More recent evidence shows that modafinil inhibits γ -aminobutyric acid release in the cerebral cortex through the possible involvement of serotonergic (5-HT₃) receptors (Ferraro et al., 1996a), leading to secondary increases in dopamine levels (Ferraro et al., 1997; Ferraro et al., 1996b; cf. Mignot, Nishino, Guilleminault, & Dement, 1994). Recently, Lin et al. (2000) proposed a hypothesis of cerebral disinhibition to account for the action of modafinil for increasing vigilance and wakefulness without the side effects of other pharmacological agents such as amphetamines (Buguet, Montmayeur, Pigeau, & Naitoh, 1995).

Despite the current lack of a substantiated theory of the underlying mechanism of modafinil, the relatively benign pharmacological effects of the drug, coupled with its vigilance-promoting properties, have stimulated two distinct avenues of research involving human participants. First, the use of modafinil has demon-

strated successful, long-term treatment of clinical sleep disorders such as idiopathic hypersomnia and narcolepsy (e.g., Bastuji & Jouvet, 1988; Billiard et al., 1994; Boivin, Montplaisir, Petit, Lambert, & Lubin, 1993; Laffont, Mayer, & Minz, 1994). Second, the potential utility of modafinil is currently being investigated in the context of sustained military operations (see Lagarde & Batejat, 1995; Lyons & French, 1991) as a potential countermeasure to the effects of extensive sleep deprivation (SD) on human cognitive performance. (For reviews of various portions of the sleep loss and performance literature, see Angus, Pigeau, & Heslegrave, 1992; Babkoff, Caspy, Mikulincer, & Sing, 1991; Dinges & Kribbs, 1991; Hockey, 1986; Krueger 1989, 1991.) In this context, several studies have documented the effectiveness of modafinil in maintaining cognitive performance during SD (Baranski, Cian, Esquive, Pigeau, & Raphel, 1998; Bensimon et al., 1991; Lagarde & Batejat, 1995; Pigeau et al., 1995).

However, modafinil is not without potential antagonistic influences on human performance. At high doses (600–800 mg/day), modafinil has shown a dose-dependent effect on blood pressure, anxiety, and insomnia (Laboratoire L. Lafon, 1994). In addition, a single-dose of 300 mg has been shown to antagonize supine pulse rate (Warot, Corruble, Payan, Weil, & Puech, 1993) and decrease the efficiency of communicated speech (Bard, Souillo, Anderson, Thompson, & Taylor, 1996). It also increases the frequency of urination (Pigeau et al., 1995), sleep onset latencies (Buguet et al., 1995), incidence of headache (Pigeau et al., 1995; Warot et al., 1993), and subjective estimates of cognitive capability (Baranski & Pigeau, 1997). However, under the dosing regimen typically prescribed for the treatment of clinical sleep disorders (i.e., 3×100 mg/24 hr), the drug is generally well tolerated (Saletu et al., 1989) and can provide effective maintenance of cognitive performance during SD (Baranski et al., 1998).

THIS STUDY

A potentially important property of modafinil, noted recently by several researchers, is that it affects thermoregulation (Bourdon, Jacobs, Bateman, & Vallerand, 1994; Brun et al., 1998; Pigeau et al., 1995). For example, Pigeau et al. reported that a single dose of modafinil (300 mg) administered at 2300 eliminated the normal fall in core temperature during the early morning hours in sleep-deprived individuals. A subsequent dose at 0800 produced a 0.4°C increase in core temperature (relative to the placebo), which was maintained throughout the following day. More generally, the thermogenic property of modafinil may be important for two reasons. First, it may limit physical work capacity in a hot environment by predisposing individuals to heat strain. Second, a disruption to thermal homeostasis is currently believed to be the principal factor that underlies the degradation of cognitive performance under thermal stress (Hancock, 1986).

To date, well over 100 published reports have examined the effect of heat stress on human cognitive performance, and excellent reviews of this literature are currently available (e.g., Bell & Greene, 1982; Grether, 1973; Hancock, 1986; Poulton, 1970; Ramsey, 1983, 1995; Wing, 1965). Perhaps the most comprehensive theoretical treatment of the extant data on thermal stress and cognitive performance was provided by Hancock (see also Hancock & Vasmatazidis, 1998; Hancock & Warm, 1989). Hancock reviewed and reinterpreted the available data from the perspective that increases (or decreases) in ambient temperature per se will not necessarily affect cognitive performance. Rather, cognitive performance degradations are contingent on dynamic disruptions to thermal homeostasis as measured by core body temperature. Working from the perspective that humans have capacity-limited attentional resources (see Kahneman, 1973; Wickens, 1980), Hancock proposed that "stress sufficient to perturb efficient homeostasis, that is, to cause an *uncontrolled* [italics added] rise or fall in deep body temperature, results in significant performance decrement" (p. 277).

In summary, modafinil appears to hold some promise as a relatively safe and effective stimulant countermeasure during sustained operations. However, modafinil has also demonstrated a thermogenic property, which has the potential to degrade cognitive performance under conditions of thermal stress. Thus, it is important to ascertain if the vigilance-enhancing properties of modafinil are mitigated when participants must perform sustained cognitive work under thermal stress. To this end, in this article we report the results of a double-blind, placebo-controlled study of the effect of modafinil on cognitive performance during 40 hr of SD in a warm environment (a companion report provides detailed coverage of thermoregulation during rest and exercise; see McLellan et al., 2002). This article focuses on simple and complex cognitive task performance and on the ability to self-monitor cognitive performance. The latter issue is important because Baranski and Pigeau (1997) reported that a large single dose of modafinil (300 mg) administered to already sleep-deprived individuals may induce overconfidence (i.e., subjective estimates of performance exceed actual cognitive performance). Thus, in this study, we also sought to examine this issue for a wider range of cognitive tasks than was examined by Baranski and Pigeau and under a dosing regimen (3×100 mg/24 hr) that is typically employed for the treatment of clinical sleep disorders (e.g., Bil-liard et al., 1994; Laffont et al., 1994).

METHOD

Participants

Participants were six graduate students from local universities who were recruited through an advertisement. All participants were men between 21 and 30 years of

age ($M = 24.7$ years) who were prescreened by a physician and classified as fit to participate if they met the following criteria: They (a) were healthy; (b) were medication free; and (c) had no allergies or hematological, cardiovascular, neurological, psychiatric, or sleep-related disorders. All participants were fully informed about the purposes of the study and the procedures to be employed, signed informed consent forms for participation, and were given a full debriefing and a medical examination on completion of the study. Participants were paid \$1,200 Canadian for their participation. The experiment was approved by the Defence and Civil Institute of Environmental Medicine (DCIEM) ethics committee for research involving human participants.

Materials

The cognitive test battery was performed on IBM-compatible laptop computers, each with an 8 × 11-in. screen and an IBM mouse, which was used as an input device on all tasks and subjective questionnaires. Participants worked independently in separate rooms (for sessions outside the climatic chamber) or in partitioned workspaces (for sessions inside the climatic chamber). An experimenter remained in the cognitive testing area at all times to answer any questions and to ensure that participants did not fall asleep during the testing period.

Procedure

The study employed a double-blind, fully within-subjects manipulation of modafinil and placebo. Participants were randomly assigned to the order of drug condition (placebo vs. modafinil) and testing phases were separated by a 5-day drug "wash-out" period. Modafinil (100 mg) or the placebo was administered at 6-hr intervals during the SD period, that is, at 0700, 1300, and 1900 of the 1st day in the climatic chamber and at 0100, 0700, 1300, and 1900 of the 2nd day in the climatic chamber. To limit modafinil intake to 300 mg/24 hr during the formal experiment, administration at 1900 was placebo in all cases. A final drug administration was given after the formal experiment at 2300 on Day 3 to examine the effect of modafinil on sleep-onset latencies and sleep architecture during the recovery sleep period. To examine the effects of modafinil on thermoregulation during exercise in the heat, the design of the study included three treadmill exercise periods, each 2-hr in duration. Exercise periods occurred at 1600 to 1800 on the 1st day in the chamber and 0400 to 0600 and 1600 to 1800 on the 2nd day in the chamber. These exercise periods were scheduled to minimize their effects on cognitive task performance; that is, all exercise periods were completed at least 2 hr before the ensuing cognitive testing sessions. A schematic representation of the experimental time line is provided in Figure 1.

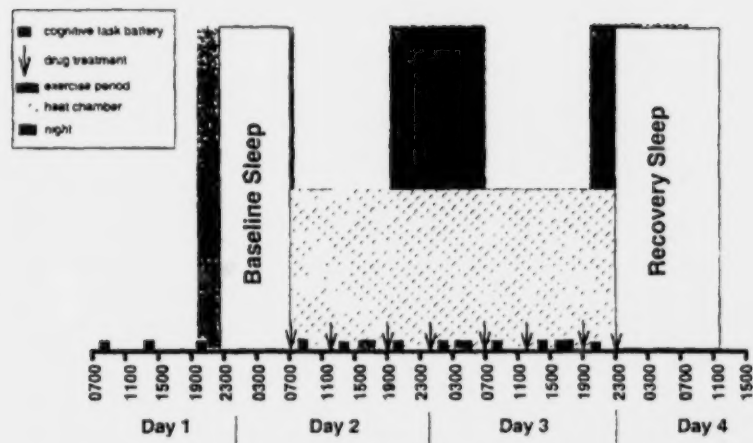


FIGURE 1 Schematic representation of the experimental timeline. Filled squares denote cognitive testing sessions, arrows denote drug or placebo administrations, hatched boxes denote exercise periods, the large hatched area denotes the period in the climatic chamber, and dark shaded areas denote evening periods.

Cognitive testing sessions lasted approximately 45 min and occurred at 6-hr intervals (i.e., 0800, 1400, 2000, and 0200). When not exercising or performing the cognitive tasks, participants read, watched TV and movies, and participated in a variety of nonphysically demanding games (e.g., cards, video games). Numerous physiological measures were recorded throughout the study (e.g., heart rate, blood pressure, and blood and urine samples); these data will be reported elsewhere by the DCIEM Thermophysiology and Operational Medicine groups. Core temperature readings were obtained continuously by a rectal thermister connected to a data logger (ACR Systems, Inc., Surrey, British Columbia, Canada).

Participants participated in 10 cognitive testing sessions per week, on each of 2 separate weeks (once with modafinil and once with placebo). Sessions 1 through 3 were performed on Day 1 in a thermoneutral environment (i.e., outside of the climatic chamber) at 6-hr intervals (i.e., 0800, 1400, and 2000). Participants slept in a thermoneutral environment on the first night from 2300 to 0600 and were introduced to the climatic chamber at 0700 of Day 2. Cognitive testing Sessions 4 through 10 were performed on Days 2 and 3 in the climatic chamber (30°C and 50% humidity) at 6-hr intervals, beginning at 0800 on Day 2. In addition to the three cognitive testing sessions that preceded each SD period, all of the participants performed for four practice sessions that were completed during a familiarization phase of the study (i.e., at least 1 week prior to the start of the formal study).

These sessions served to stabilize performance on the various tasks and, thus, to minimize the effects of practice on cognitive task performance.

Cognitive Test Battery

The cognitive test battery included a subset of tasks, which have been used extensively in previous sleep loss and performance studies conducted at DCIEM (e.g., Angus & Heslegrave, 1985; Baranski, Pigeau, & Angus, 1994; Pigeau et al., 1995). The tasks were selected for the study to investigate a diverse range of fundamental cognitive processes and to allow comparison with findings obtained in previous studies. The tasks that comprised the cognitive test battery were always performed in the same order and included the following measures.

Subjective questionnaires (approximately 3 min). The questionnaire included four items, which probed the participants' current level of mental and physical fatigue, motivation, and mood. Each question involved a visual analog scale from 1 to 10, which was anchored at both ends by a short verbal description (e.g., *not at all tired* vs. *very tired*). The participant "hooked" a visual pointer on a sliding scale with the computer mouse and dragged the pointer on the monitor to the appropriate location on the scale.

Four-choice serial reaction time (SRT; 3 min). For each trial, four response buttons (P, G, L, and S) were presented on the computer monitor in a square configuration (i.e., two above and two below). Directly above the displayed letters, a probe letter (P, G, L, or S) was presented. The participant's task was to move a visual pointer with the mouse over the corresponding probe letter and to depress the mouse button as quickly and as accurately as possible. The probe letter varied on each trial and was randomly generated by the program. Response times were recorded from the appearance of the probe letter to the depression of the response button on the mouse.

Mental addition (ADD; 9 min). The addition task required participants to add a random sequence of eight numbers (between 1 and 16), which were presented on the computer monitor at a rate of 1 number per 1.25 sec. The sequence was terminated by the presentation of a visual prompt ($\Rightarrow$) at which time participants typed in their response using the mouse and a visual keypad presented on the monitor. Response times and response accuracy were measured for each trial.

Detection of repeated numbers (DRN) vigilance task (8 min). The DRN was a vigilance task that required participants to detect by pressing a key with the mouse, when two 3-digit numbers occurred in succession. Three-digit numbers were presented at a rate of 1 per second. In total, eight repeated numbers occurred

randomly distributed within each minute of the task. Correct detections occurred when the participant pressed a key with the mouse within 2 sec of a repeated number. Misses occurred when repeated numbers were presented but the mouse button was not pressed; false alarms occurred when the mouse button was pressed but successive numbers were not presented.

Logical reasoning task (LRT; 3 min). On each trial of the LRT, a pair of letters was presented at the top of the screen: A B or B A. Directly below the pair of letters was a statement concerning the spatial arrangement of the letters (e.g., "A precedes B"; "B does not follow A"). The participant's task was to determine if the statement was true or false and to press with the mouse the appropriate response button (T or F) on the screen. Response time and response accuracy were measured on each trial.

Visual perceptual comparison (5 min). The comparison task required the relative judgment of line length. Each trial began with the presentation of an instruction ("LONGER" or "SHORTER"), which was displayed near the top of the computer monitor. One second later, a visual display appeared that consisted of two horizontal lines, divided by one short vertical line. The display remained on the screen until the participant responded. The participant's task was to determine which of the two lines was longer or shorter, depending on the instruction; participants responded by depressing either the left or the right button on the mouse to indicate that the left or right line was longer or shorter. Four levels of judgment difficulty were randomly presented to the participants; the difficulty was defined a priori on the basis of the ratio of the longer to the shorter line: 1.01, 1.03, 1.05, and 1.07. All lines appeared black on a white background. Participants were encouraged to respond as quickly and as accurately as possible. Response time and response accuracy were recorded on each trial.

Multitasking (SYNWORK; 8 min). SYNWORK is a computer-based multitasking environment developed by Elsmore (1994). The environment includes four subtasks: short-term memory, arithmetic processing, and visual and auditory monitoring. For this study, the auditory monitoring task was disabled, thus requiring only three subtasks. Participants obtained points by correctly identifying letters from a memorized string, by correctly adding two 4-digit numerals, and by resetting a drifting visual pointer before it reached a boundary. The participants were to obtain as high a total composite score as possible in each session of the task, which was engaging, competitive, and of a higher level of cognitive complexity than the others.

Subjective questionnaires (approximately 3 min). The cognitive task battery concluded with an additional presentation of the subjective questionnaires dis-

cussed previously. This permitted a view of the effects of performing the cognitive task battery on mood, motivation, and fatigue levels.

Self-monitoring. Four of the cognitive tasks reported previously permitted a quantitative index of response accuracy (i.e., percentage of correct responses). These were the ADD task, the perceptual comparison task, the LRT, and the DRN (vigilance) task. To assess the extent to which participants were able to accurately assess their own cognitive abilities during SD, each of the four aforementioned tasks was preceded with a single question that asked participants to estimate their percentage of correct responses (i.e., a pretask estimate). In addition, each task was followed by a similar question that asked participants to estimate the percentage of responses that they answered correctly (i.e., a posttask estimate). Participants' self-monitoring ability was assessed by comparison of the subjective estimates of performance with actual performance accuracy. When the estimates exceeded or fell below actual performance, we concluded that participants were overconfident or underconfident in their assessments, respectively. When assessments closely matched performance, we concluded that participants were "well calibrated" (see Baranski & Pigeau, 1997; Baranski et al., 1994). Baranski and Pigeau showed that a large single dose of modafinil (300 mg) induced overconfidence in already sleep-deprived participants. Thus, this study sought to examine this effect under a preventative dosing regimen (i.e., 3×100 mg/24 hrs).

RESULTS

The results are reported in four sections. In the first, we provide a view of core body temperatures, comparing the modafinil and placebo trials with the thermoneutral control day. In the second, we report on the effects of the drug manipulation on subjective estimates of mood, performance, and physical and mental fatigue. The third section provides a view of the effects of the drug manipulation on cognitive performance, and the fourth section presents the results of the self-monitoring analysis. Unfortunately, the data set for one participant was incomplete because several sessions were lost due to a computer problem. Accordingly, all analyses to be reported are based on the complete data sets of five participants.

Core Temperature Data

Figure 2 provides a plot of core body temperature for four of the five participants in this study (the data for one participant were unreliable for several sessions due to equipment malfunction). The curves for the modafinil and placebo trials (upper curves) denote data obtained on Days 2 and 3 inside the climatic chamber. The curve for the thermoneutral control trial (lower curve) denotes data obtained out-

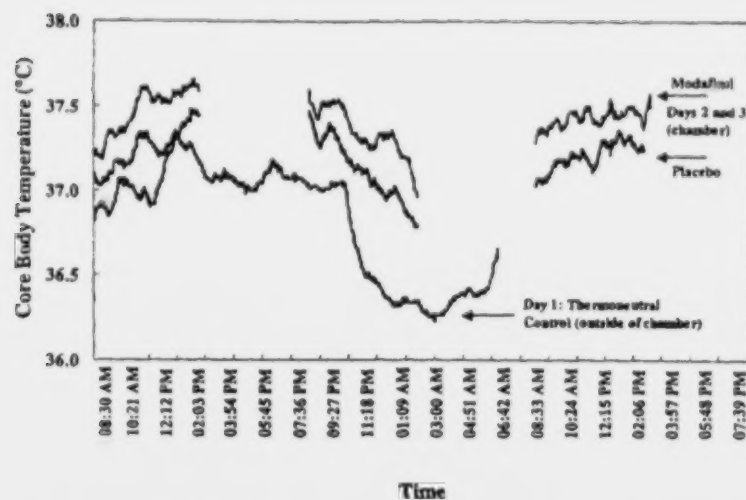


FIGURE 2 Core body temperatures ($n = 4$) The lower curve shows data for Day 1 in a thermoneutral (control) environment. The top curves are for the modafinil and placebo trials during Days 2 and 3 in the climatic chamber. Discontinuities in the modafinil and placebo curves denote exercise periods.

side of the climatic chamber on Day 1 of the 1st week of testing. The data clearly show that, relative to Day 1 in a thermoneutral control environment, core temperature increased on Days 2 and 3 on exposure to the climatic chamber for both the placebo and the modafinil trials. In addition, the thermogenic effect of modafinil is also clearly evident; throughout, core temperatures were elevated for the modafinil trial as compared to the placebo trial. The discontinuities in the graph denote exercise periods during which cognitive testing did not occur (for a complete view of the effects of exercise on core temperature, see our companion article, McLellan et al., 2002).

A repeated measures analysis of variance (ANOVA) was conducted with Drug Condition (control vs. placebo vs. modafinil) and Time Interval as within-subject factors. Although temperature was recorded continuously, for purposes of analysis, we partitioned the time scale into six intervals, during which data were collected for each drug condition and which coincided for the most part with the cognitive testing periods. The six intervals were 0830 to 1030, 1030 to 1230, 1230 to 1430, 2030 to 2230, 2230 to 0030, and 0030 to 0230.

An ANOVA revealed highly significant main effects of drug condition, $F(2, 6) = 57.64, p < .0001$, and time interval, $F(5, 15) = 7.33, p < .002$, but no interaction.

The significant effects denote, respectively, reliable differences among the drug conditions and the clear circadian effects evident in the core temperature data. Post hoc analyses confirmed reliable differences between the control and placebo trials ($p < .0005$), the control and modafinil trials ($p < .0001$), and the placebo and modafinil trials ($p < .009$). Taken together, these findings serve to confirm that participants were under thermal stress while in the warm environment and that modafinil produced additional thermal stress (relative to the placebo trial). More important, the lack of a reliable Drug $\times$ Time Interval interaction indicates that participants in both the modafinil and placebo conditions were able to maintain thermal homeostasis, albeit at a higher level than was the case in the thermoneutral control condition.

Subjective Measures

Results of the subjective questionnaires, administered before and after each session, were analyzed by repeated measures ANOVA with Time of Testing (pretest vs. posttest), Drug Condition (modafinil vs. placebo), and Session (10 levels) as within-subject factors. If the conventional ANOVA revealed reliable drug or Drug $\times$ Session effects, then Fisher LSD post hoc comparisons were performed to identify the source of the differences.

Mental fatigue. Figure 3 provides a plot of subjective estimates of mental fatigue. The plot shows a clear trend toward greater fatigue with increasing SD, as well as a difference between the drug conditions. Indeed, an ANOVA confirmed main effects of session, $F(9, 36) = 10.1, p < .0001$, and drug, $F(1, 4) = 13.6, p < .025$, but no interaction between the two. Post hoc comparisons revealed a difference between placebo and modafinil at 1400 on Day 3 ($p = .05$) and a marginal difference at 0800 on Day 3 ($.05 < p < 1$). The only other effect to achieve statistical significance was the interaction between time of testing and sessions, $F(9, 36) = 2.33, p < .05$. Fatigue levels were increased on completion of the cognitive test battery for the early sessions but not for the later sessions.

Physical fatigue. Subjective estimates of physical fatigue were very similar to those reported for the mental fatigue scale. The main effect of session was highly reliable, $F(9, 36) = 10.2, p < .0001$, and the effect of drug condition was marginally reliable, $F(1, 4) = 6.8, p = .059$.

Mood. Mood ratings were generally high, confirming our personal observations that these participants were quite amicable. In addition, they displayed no drug effect and only a small reduction in mood throughout the course of the study. Accordingly, the only reliable effect was due to session, $F(9, 36) = 2.9, p < .02$.

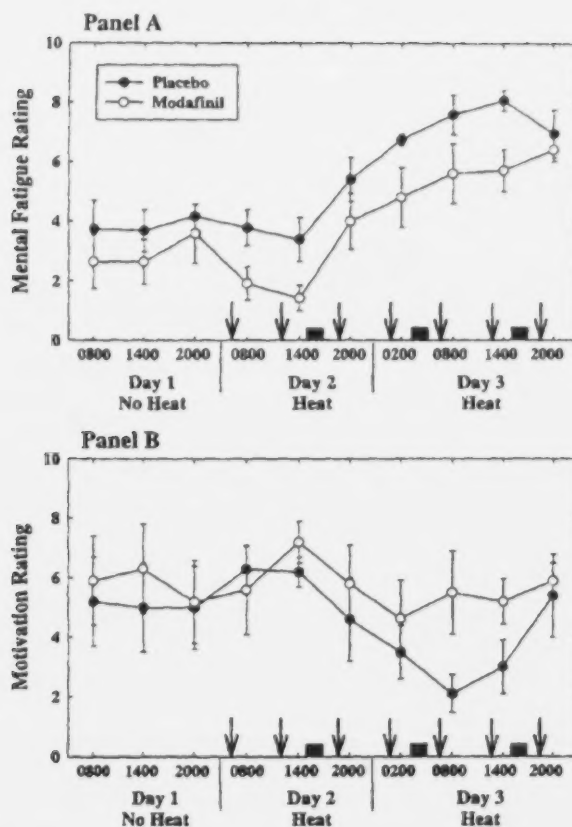


FIGURE 3 Subjective ratings of mental fatigue (Panel A) and motivation (Panel B) for the placebo and modafinil trials. Filled squares denote exercise periods, arrows denote drug administrations, and error bars denote the standard error of the mean across participants

Motivation. Figure 3 provides a plot of subjective estimates of motivation. The plot is revealing in that the modafinil condition showed no appreciable loss throughout the study, whereas the placebo condition displayed a clear reduction in motivation during the SD period. These results were confirmed by a marginal main effect of drug, $F(1, 4) = 6.95, p = .058$, which was qualified by a significant Drug $\times$ Session interaction, $F(9, 36) = 2.51, p < .025$. No other effects were reliable. Post

hoc comparisons revealed that the modafinil and placebo trials differed reliably at 0800 on Day 3 ($p < .002$) and at 1400 on Day 3 ($p < .035$).

Summary of the subjective measures. Overall, the participants' mood states remained fairly positive throughout the study and were independent of drug condition. Fatigue levels were higher in the placebo condition, particularly during the SD period. Most notably, subjective estimates of motivation were clearly distinguished from mood in that they displayed a clear interaction between session and drug condition.

Cognitive Performance Measures

Results of the cognitive tasks were analyzed by a repeated measures ANOVA with Drug Condition (2 levels: modafinil vs. placebo) and Session (10 levels) as within-subject factors. Again, Fisher LSD post hoc comparisons were performed when the conventional ANOVA revealed reliable drug or Drug $\times$ Session effects. More important, inherent differences among the various cognitive tasks necessitated the examination of different dependent measures. For example, the SRT task and the LRT were performed with a high degree of accuracy. Accordingly, in the absence of speed-accuracy tradeoff effects, in this study we examined the number of correct responses per minute, which provided a composite measure of response speed and response accuracy. For the ADD and visual comparison (CMP) tasks, both response accuracy and response time were analyzed. For the DRN (vigilance) task, responses had to be provided within a specific period and, as such, the number of correct detections, misses, and false alarms provided the critical measures. Finally, for the SYNWORK task (multitasking), the total composite score was used as the dependent measure.

SRT. Response times greater than 3 standard deviations from the mean were trimmed as outliers because examination of the raw data indicated that these trials were undoubtedly due to the influence of breaks, pauses, drinking, or other activities and possibly even a few lapses. However, the relative proportion of these causes could not be precisely delineated. This accounted for 496 of the 22,164 trials (2.24%). The number of correct responses per minute for the placebo and modafinil trials are presented in Figure 4. The plot shows that performance for the early sessions was equivalent for the placebo and modafinil conditions and was totally unaffected by the 1st full day in the hot environment; that is, performance during Sessions 4 through 6 in the chamber was virtually identical to performance during Sessions 1 through 3 in the thermoneutral environment. After 2000 of Day 2, however, performance on the placebo trial began to decline with increasing SD. By comparison, performance on the modafinil trial showed less degradation from 2000 to 0800. In addition, there was a recovery of performance under modafinil

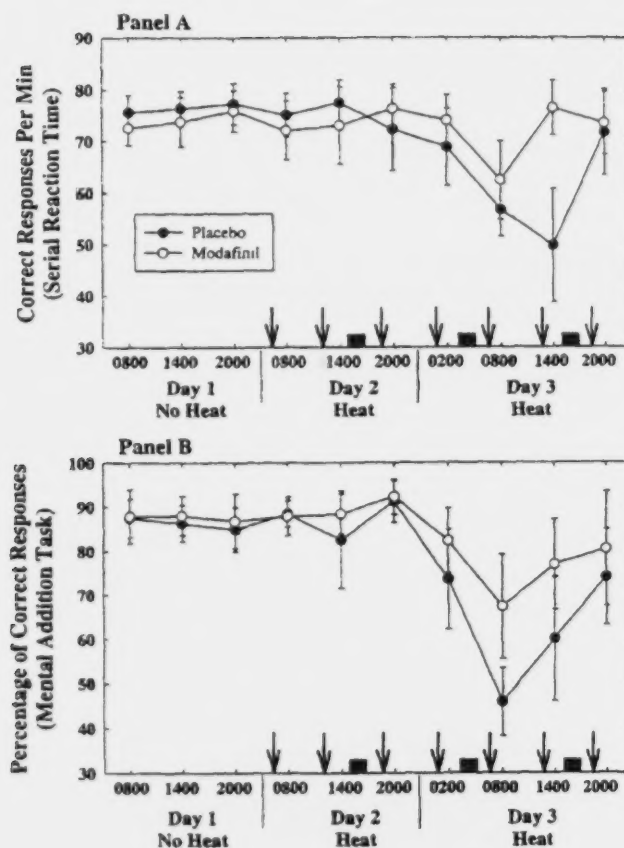


FIGURE 4 Correct responses per min on the serial reaction time task (Panel A) and the percentage of correct responses on the mental addition task (Panel B) for the placebo and modafinil trials. Filled squares denote exercise periods, arrows denote drug administrations, and error bars denote the standard error of the mean across participants

but not placebo at 1400 on Day 3. An ANOVA revealed no main effect of drug, a clear effect of session, $F(9, 36) = 5.01$, $p < .0003$, and a significant Drug $\times$ Session interaction, $F(9, 36) = 4.08$, $p < .002$. The last effect confirmed a reliable difference between modafinil and the placebo during the latter stages of the SD period. Indeed, post hoc comparisons revealed a reliable difference between the modafinil and placebo trials at 1400 of Day 3 ($p < .0001$).

ADD. Trials on which response times were greater than 3 standard deviations from the mean, which were trimmed as outliers, accounted for 139 of the 2,107 trials (6.59%). An analysis conducted on the response time measure revealed no main effects or interactions. Figure 4 shows the percentage of correct responses for the ADD task. The findings closely parallel those reported for the SRT task, except that the performance decline due to SD was more pronounced for both placebo and modafinil, and the difference between modafinil and the placebo was evident for a longer duration. Accordingly, the main effects of session, $F(9, 36) = 5.8, p < .0001$, and drug, $F(1, 4) = 10.5, p < .04$, were reliable, but the interaction was not. Post hoc comparisons revealed reliable differences between modafinil and the placebo at 0800 on Day 3 ($p < .006$) and at 1400 on Day 3 ($p < .03$).

DRN vigilance. Figure 5 shows the number of correct detections per minute for the DRN vigilance task (recall that the maximum number of detections was eight per minute). Once again, the placebo condition displayed a pronounced decline in performance with increasing sleep loss, whereas performance under modafinil showed only a minor decrement. An ANOVA revealed significant main effects of drug, $F(1, 4) = 8.1, p < .05$, and session, $F(9, 36) = 5.16, p < .0001$, and a reliable Drug $\times$ Session interaction, $F(9, 36) = 3.15, p < .007$, with the last effect confirming a more pronounced difference between the placebo and modafinil during the latter stages of the SD period. Indeed, post hoc comparisons revealed reliable differences between the placebo and modafinil at 2000 of Day 2 ($p < .004$), 0200 of Day 3 ($p < .003$), 0800 of Day 3 ($p < .0001$), 1400 of Day 3 ($p < .004$), and 2000 of Day 3 ($p < .02$). Finally, an ANOVA on the number of false alarms revealed no main effects or interaction, confirming that the results reported in Figure 5 were due exclusively to errors of omission (i.e., misses).

Logical reasoning. Trials on which response times were greater than 3 standard deviations from the mean, which were trimmed as outliers, accounted for 128 of the 5,125 trials (1.95%). Figure 5 provides a plot of the number of correct responses per minute for the placebo and modafinil trials. The plot shows once again that performance for the early sessions was equivalent for the placebo and modafinil conditions and was unaffected by the 1st full day in the hot environment. After 2000 of Day 2, however, performance on the placebo and modafinil trials began to decline, although the decline was clearly larger for the placebo trial. An ANOVA revealed a marginal effect of drug, $F(1, 4) = 5.38, p = .08$; a clear effect of session, $F(9, 36) = 8.1, p < .0001$; and a Drug $\times$ Session interaction, $F(9, 36) = 2.15, p = .05$. Post hoc comparisons revealed reliable differences between placebo and modafinil at 2000 on Day 2 ($p < .02$), 0800 on Day 3 ($p < .005$), 1400 on Day 3 ($p < .005$), and 2000 on Day 3 ($p < .02$).

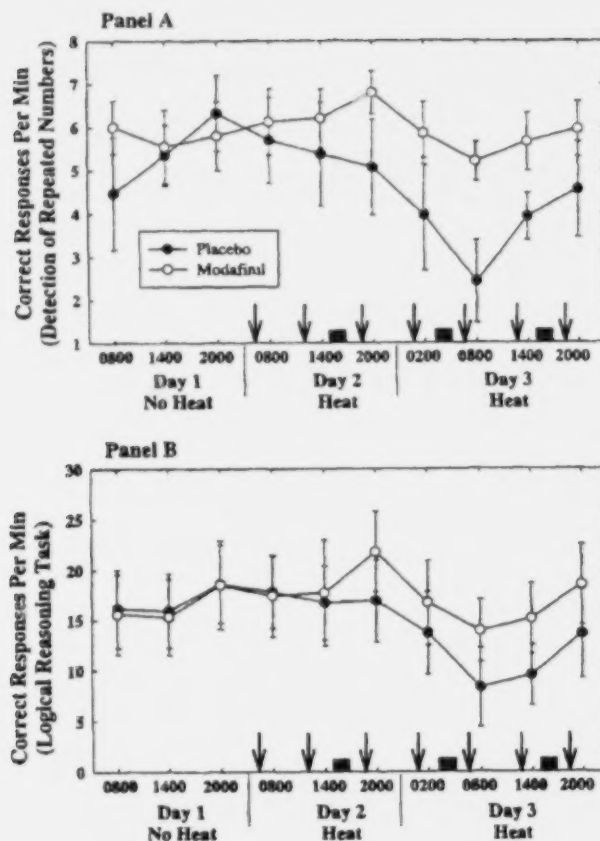


FIGURE 5 Correct responses per minute on the detection of repeated numbers vigilance task (Panel A) and the logical reasoning task (Panel B) for the placebo and modafinil trials. Filled squares denote exercise periods, arrows denote drug administrations, and error bars denote the standard error of the mean across participants

Perceptual comparison. Trials on which response times were greater than 3 standard deviations from the mean were trimmed as outliers, and these accounted for 218 of the 6,376 trials (3.42%). As with the ADD task, an analysis of the response times revealed no main effects or interactions. Figure 6 provides a view of the percentage of correct responses for the perceptual comparison task. In contrast to the other tasks, performance under the placebo and modafinil was virtually identical.

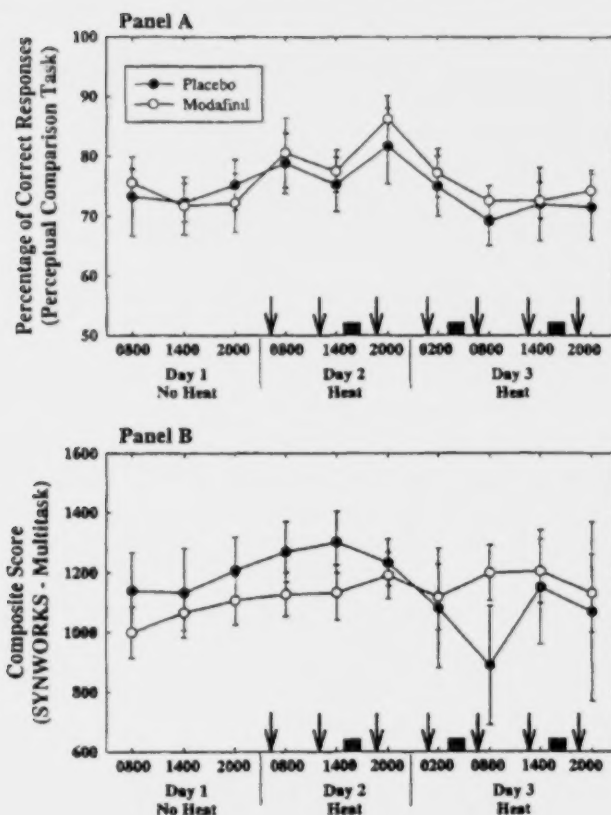


FIGURE 6 Percentage of correct responses on the perceptual comparison task (Panel A) and the composite score on the SYNWORK multitask (Panel B) for the placebo and modafinil trials. Filled squares denote exercise periods, arrows denote drug administrations, and error bars denote the standard error of the mean across participants.

tical (i.e., both showed a small but noticeable decline with increasing sleep loss). Indeed, the only result to achieve statistical significance was the main effect of session, $F(9, 36) = 2.23, p < .05$.

Multitasking (SYNWORK). Figure 6 provides the results for the composite score on the SYNWORK multitask. Performance under the influence of modafinil was well maintained throughout the protocol, whereas performance under the pla-

cebo showed a notable decline with increasing SD, observations that were confirmed by a reliable Drug $\times$ Session interaction, $F(9, 36) = 2.3, p < .04$. Neither of the main effects approached significance. Post hoc comparisons revealed that the placebo and modafinil differed only at 0800 of Day 3 ($p < .003$).

Summary of the cognitive measures. Although modafinil (3×100 mg/24 hr) was not sufficient to maintain cognitive performance at baseline levels throughout the experimental protocol, the degradation due to sleep loss was significantly reduced relative to the placebo. The one exception was the perceptual comparison task (see also Baranski et al., 1998), which displayed a relatively small overall reduction in performance due to sleep loss. This finding is significant because the perceptual comparison task was the only one in the cognitive test battery that did not require either sustained attention or working memory resources.

Self-Monitoring Analyses

Figure 7 plots the self-monitoring data separately for the trials using modafinil (top panel) and the placebo (lower panel). The data were averaged over the four tasks that permitted a quantitative index of response accuracy (percentage correct), which could be compared directly to subjective estimates of performance (i.e., CMP, ADD, LRT, and DRN). The mean percentage of correct responses is represented in each figure by filled circles; the mean pretask and posttask estimates are denoted by open circles and triangles, respectively. Three notable findings are evident in these plots. First, in the placebo trial, performance declined during the SD period; during the modafinil trial, the performance decline was reduced but clearly not eliminated. Second, in the placebo trial, participants displayed excellent self-monitoring of performance (i.e., their estimates accurately tracked their overt performance; Baranski et al., 1994; Baranski & Pigeau, 1997; see Dorrian, Lamond, & Dawson, 2000). Finally, in contrast to the findings of Baranski and Pigeau (1997), participants displayed good self-monitoring on the modafinil trial as well.

A repeated measures ANOVA was conducted with the difference between estimated (i.e., pretask and posttask estimates) and observed performance (i.e., percentage correct) as the dependent measures. That is, positive differences on this statistic denoted overconfidence in the assessment, negative differences denoted underconfidence, and no difference denoted perfect calibration (see Baranski & Petrusic, 1994, 1998, 1999). Drug (2 levels: modafinil vs. placebo), Session (10 levels), and Task (4 levels: CMP, LRT, ADD, and DRN) were within-subject factors. Overall, participants displayed remarkably good calibration during the modafinil and the placebo trials (e.g., the mean difference score was 0.2% for the placebo and 0.85% for modafinil). Thus, in replication of the findings reported by Baranski et al. (1994; see also Dorrian et al., 2000), participants could accurately self-monitor their performance when sleep deprived.

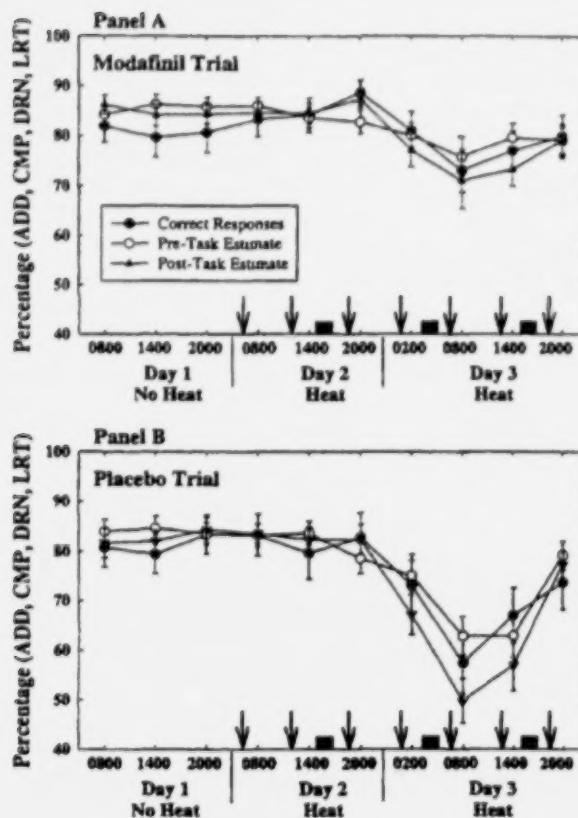


FIGURE 7 Mean percentage of correct responses (filled circles), pretask estimates (open circles), and posttask estimates (triangles) for the modafinil (Panel A) and the placebo (Panel B) trials. Filled squares denote exercise periods, arrows denote drug administrations, and error bars denote the standard error of the mean across participants

The ANOVA revealed a significant effect of task for both the pretask and posttask estimates, $F(3, 12) = 4.57, p < .05$, and $F(3, 12) = 4.84, p < .05$, respectively. Post hoc comparisons revealed that, overall, participants were slightly underconfident on the LRT (-9.8%) and slightly overconfident on the vigilance task (8.5%) and showed good calibration on the ADD and comparison tasks. Only two other effects were reliable. The first was a main effect of session for the posttask estimates, $F(9, 36) = 3.39, p < .005$; participants were generally well cali-

brated across sessions but showed a trend toward underconfidence during the SD sessions (i.e., Sessions 7, 8, and 9 were -4.8, -4.9, and -6.9%, respectively). A related finding in a different context was recently reported by Blagrove and Akehurst (2000). The only other effect to reach statistical significance was an interaction between task and drug for the posttask estimates, $F(3, 12) = 3.52$, $p < .05$. Participants in the placebo trial were more underconfident on the LRT (-16.0 vs. -8.4%) but were more overconfident on the vigilance task (11.3 vs. 6.3%). However, because these effects were all in the same direction and did not interact with session, we do not discuss their practical significance further.

DISCUSSION

This study examined the effect of modafinil on cognitive performance during 40 hr of SD in a warm environment. Three specific questions related to cognitive performance were addressed: (a) the effect of a dynamic change in core temperature *per se*, (b) the effectiveness of modafinil to counteract the performance degradations associated with fatigue due to sleep loss, and (c) the effect of modafinil on the ability to self-monitor cognitive performance.

Effects of Changes in Core Temperature on Cognitive Performance

The conditions of this study were clearly sufficient to produce thermal stress; that is, core temperatures were significantly higher during the 1st day of the placebo trial than during the preceding control day in the thermoneutral environment. In addition, the thermogenic effect of modafinil further increased core temperature, relative to placebo. More important, although participants were under thermal stress, they were able to maintain thermal homeostasis. In support of Hancock's (1986) view, cognitive performance was completely unaffected during the 1st day in the climatic chamber; performance on the modafinil and the placebo trials was identical to that observed during the preceding control day. Accordingly, the findings from Day 2 of this study (i.e., the 1st day in the climatic chamber) provide support for Hancock's view that thermal stress *per se* is insufficient to produce cognitive performance degradations.

Effects of Modafinil on Cognitive Performance During SD

For the placebo trial, cognitive performance displayed the expected decline during the evening SD period. This decline was attenuated but not eliminated by the modafinil regimen (3×100 mg/24 hr). Indeed, as is evident in Figure 7, a comparison of response accuracy for Sessions 1 through 6 (baseline) to that for Session 8

(circadian low) showed a 12% reduction on the modafinil trial as compared to a 30% reduction on the placebo trial. Hence, we conclude that modafinil provides effective but not complete maintenance of cognitive performance during SD. It is unclear to what extent the 12% reduction in performance on the modafinil trial was due to the warm environment *per se*. The study was conducted with specific applied (physical and cognitive) questions in mind and, thus, lacked the necessary control conditions to answer this question. However, given that the performance on Day 1 in the chamber was completely unaffected by the warm environment, we can state with some confidence that these findings would generalize to a thermoneutral environment.

More generally, these findings are difficult to interpret with respect to the potential combined effects of SD and thermal stress. In two previous studies that examined the combined effects of heat stress and sleep loss on cognitive performance (Pepler, 1959; Poulton, Edwards, & Colquhoun, 1974), there was little or no effect of the combination of the stressors beyond that observed for each stressor in isolation. However, in both studies, participants were exposed to a hot environment after a night of sleep loss in a thermoneutral environment, the duration of heat exposure was not specified, and core temperature data were not provided. Thus, the findings of the previous studies are difficult to evaluate with respect to Hancock's (1986) proposal. Nevertheless, the issue of combined stressors, such as sleep loss and thermal stress, has real-world application, as discussed in the introduction of this article (see also the discussion by Babkoff & Krueger, 1992).

A final issue that merits consideration concerns the nature of the relation between modafinil's thermogenic and vigilance-enhancing properties. Although it is clear that both effects are regulated by central nervous system stimulation, it is important to consider that some portion of modafinil's vigilance-enhancing effect may derive from its thermogenic property. For example, it is well known that alertness declines and the propensity to sleep increases as core temperature decreases (Barrett, Lack, & Morris, 1993; cf. Murphy & Campbell, 1997). In addition, it is also known that evening sleepiness and sleep onset can be delayed by exogenous factors that increase core temperature, such as certain foods (Edwards, Montgomery, Colquhoun, Jordan, & Clark, 1992), bright light (Dijk, Cajochen, & Borbely, 1991), and exercise (Mizuno, Asano, & Okamoto, 1998). Hence, part of the reason for modafinil's vigilance-enhancing effects could be related to the fact that it attenuates the circadian drop in core temperature, thus delaying the associated decline in alertness. On the other hand, whereas core temperature is strongly regulated by circadian variation of the thermoregulatory set point (Cabanac, Hildebrandt, Massonet, & Strempel, 1976), cognitive performance is regulated by both circadian and monotonic (i.e., duration of sleep loss) influences (see Babkoff et al., 1991). Accordingly, if there exists a direct effect of modafinil's thermogenic property on vigilance, it will likely become less prominent as the duration of SD increases.

Effect of Modafinil on the Ability to Self-Monitor Cognitive Performance

This study has shown that modafinil ($3 \times 100\text{mg}/24\text{ hr}$) does not have an antagonistic effect on the ability to judge one's own cognitive capabilities, a finding that contrasts with those reported by Baranski and Pigeau (1997). However, there are a number of important differences between the two studies. First, this study employed a within-subject design, whereas the Baranski and Pigeau study involved a between-subjects design. Hence, this study may have permitted a clearer reference point for self-monitoring. Second, this study required self-monitoring assessments only intermittently (i.e., at 6-hr intervals), whereas the Baranski and Pigeau study involved a continuous cognitive work paradigm. Hence, subjective estimates of performance degradations may have been more salient in this study. Finally, and most notably, Baranski and Pigeau administered a large single dose (300 mg) to participants who were already sleep deprived to examine the extent to which the stimulant could recuperate cognitive performance deficits once they had already occurred. In this study, by contrast, we employed a continuous, low-dose regimen, typical of that employed in clinical treatment of narcolepsy, in an effort to examine the extent to which modafinil could maintain performance through a 40-hr SD period. Apparently, modafinil per se does not affect one's self-monitoring ability, although large single doses may have unwanted side effects (as reviewed in the introduction). Given modafinil's generally effective vigilance-promoting properties and its tolerance level at low doses, it may provide a relatively safe and effective countermeasure to the effects of fatigue due to sleep loss in sustained operational contexts.

ACKNOWLEDGMENTS

We thank Andrea Hawton for invaluable technical support, Marc Grushcow and NTT, Inc., for programming the portable cognitive test battery, Tonya Stokes for assistance with the data analyses, Trish Unruh for assistance with the data collection, and Gerald Krueger and two reviewers for their helpful comments.

REFERENCES

- Angus, R., & Heslegrave, R. (1985). Effects of sleep loss on sustained cognitive performance during a command and control simulation. *Behavioral Research Methods, Instruments, and Computers*, 17, 55-67.
- Angus, R., Pigeau, R., & Heslegrave, R. (1992). Sustained operations studies: From the field to the laboratory. In C. Stampi (Ed.), *Why we nap: Evolutionary, chronobiology, and functions of polyphasic and ultrashort sleep* (pp. 217-241). Boston: Birkhauser.

- Babkoff, H., Caspy, T., Mikulincer, M., & Sing, H. (1991). Monotonic and rhythmic influences: A challenge for sleep deprivation research. *Psychological Bulletin*, 109, 411-428.
- Babkoff, H., & Krueger, G. (1992). Use of stimulants to ameliorate the effects of sleep loss during sustained performance. *Military Psychology*, 4, 191-205.
- Baranski, J. V., Cian, C., Esquivé, D., Pigeau, R. A., & Raphael, C. (1998). Modafinil during 64 hr of sleep deprivation: Dose-related effects on fatigue, alertness, and cognitive performance. *Military Psychology*, 10, 173-193.
- Baranski, J. V., & Petrusic, W. M. (1994). The calibration and resolution of confidence in perceptual judgments. *Perception & Psychophysics*, 55, 412-428.
- Baranski, J. V., & Petrusic, W. M. (1998). Probing the locus of confidence judgments: Experiments on the time to determine confidence. *Journal of Experimental Psychology: Human Perception and Performance*, 24, 929-945.
- Baranski, J. V., & Petrusic, W. M. (1999). Realism of confidence in sensory discrimination. *Perception & Psychophysics*, 61, 1369-1383.
- Baranski, J. V., & Pigeau, R. (1997). Self-monitoring cognitive performance during sleep deprivation: Effects of modafinil, d-amphetamine and placebo. *Journal of Sleep Research*, 6, 84-91.
- Baranski, J. V., Pigeau, R., & Angus, R. (1994). On the ability to self-monitor cognitive performance during sleep deprivation: A calibration study. *Journal of Sleep Research*, 3, 36-44.
- Bard, E. G., Sotillo, C., Anderson, A. H., Thompson, H. S., & Taylor, M. M. (1996). The DCIEM map task corpus: Spontaneous dialogue under sleep deprivation and drug treatment. *Speech Communication*, 20, 71-84.
- Barrett, J., Lack, L., & Morris, M. (1993). The sleep-evoked decrease of body temperature. *Sleep*, 16, 93-99.
- Bastuji, H., & Jouvet, M. (1988). Successful treatment of idiopathic hypersomnia and narcolepsy with modafinil. *Progress in Neuropsychopharmacology and Biological Psychiatry*, 12, 695-700.
- Bell, P. A., & Greene, T. C. (1982). Thermal stress: Physiological, comfort, performance, and social effects of hot and cold environments. In G. W. Evans (Ed.), *Environmental stress* (pp. 75-104). Cambridge, England: Cambridge University Press.
- Beaumont, G., Benoit, D., Lacomblez, L., Weiller, E., Warot, D., Weil, J., & Puech, A. (1991). Antagonism by modafinil of the psychomotor and cognitive impairment induced by sleep deprivation in 12 healthy volunteers. *European Journal of Psychiatry*, 6, 93-97.
- Billard, M., Besset, A., Montplaisir, J., Laffont, F., Goldenberg, F., Weill, J., & Lubin, S. (1994). Modafinil. A double-blind multicentric study. *Sleep*, 17(Suppl. 8), 107-112.
- Blagrove, M., & Akehurst, L. (2000). Effects of sleep loss on confidence-accuracy relationships for reasoning and eyewitness memory. *Journal of Experimental Psychology: Applied*, 6, 59-73.
- Bovim, D., Montplaisir, J., Petit, D., Lambert, C., & Lubin, S. (1993). Effect of modafinil on symptomatology of human narcolepsy. *Clinical Neuropharmacology*, 16, 46-53.
- Bourdon, L., Jacobs, I., Bateman, W., & Vallerand, A. (1994). Effect of modafinil on heat production and regulation of body temperatures in cold-exposed humans. *Aviation, Space, and Environmental Medicine*, 65, 999-1004.
- Brun, J., Chamba, G., Khalifallah, Y., Girard, P., Boissy, I., Bastuji, H., Sassolas, G., & Claustrat, B. (1998). Effect of modafinil on plasma melatonin, cortisol and growth hormone rhythms, rectal temperature, and performance in healthy participants during 36h sleep deprivation. *Journal of Sleep Research*, 4, 229-241.
- Buguet, A., Montmayeur, A., Pigeau, R., & Naitoh, P. (1995). Modafinil, d-amphetamine and placebo during 64 hours of sustained mental work: II. Effect on two nights of recovery sleep. *Journal of Sleep Research*, 4, 229-241.
- Cahanac, M., Hildebrandt, G., Massonet, B., & Strempel, H. (1976). A study of the eucythermal cycle of behavioral temperature regulation in man. *Journal of Physiology*, 257, 275-291.

- Dijk, D. J., Cajochen, C., & Borbely, A. (1991). Effect of a single 3-hour exposure to bright light on core temperature and sleep in humans. *Neuroscience Letters*, 121, 59-62.
- Dinges, D., & Knbits, N. (1991). Performing while sleepy: Effects of experimentally-induced sleepiness. In T. Monk (Ed.), *Sleep, sleepiness, and performance* (pp. 97-128). Chichester, England: Wiley.
- Dorman, J., Lamond, N., & Dawson, D. (2000). The ability to self-monitor performance when fatigued. *Journal of Sleep Research*, 9, 137-144.
- Duteil, J., Rambert, F., Pessonnier, J., Gombert, R., & Assous, E. (1979). A possible alpha adrenergic mechanism for drug (CRL 40028)-induced hyperactivity. *European Journal of Pharmacology*, 59, 121-127.
- Duteil, J., Rambert, F., Pessonnier, J., Hermant, J. F., Gombert, R., & Assous, E. (1990). Central alpha 1 adrenergic stimulation in relation to the awakening activity of modafinil: Behavioral studies in laboratory animals. *European Journal of Pharmacology*, 180, 49-58.
- Edwards, S. J., Montgomery, I. M., Colquhoun, E. Q., Jordan, J. E., & Clark, M. G. (1992). Spicy meal disturbs sleep: An effect of thermoregulation? *International Journal of Psychophysiology*, 13, 97-100.
- Elsmore, T. (1994). SYNWORK1: A PC-based tool for assessment of performance in a simulated work environment. *Behavior Research Methods, Instruments, and Computers*, 26, 421-426.
- Ferraro, L., Antonelli, T., O'Connor, W. T., Tanganelli, S., Rambert, F., & Fuxe, K. (1997). Modafinil: An antinausea drug with different neurochemical profile to d-amphetamine and dopamine uptake blockers. *Biological Psychiatry*, 42, 1181-1183.
- Ferraro, L., Tanganelli, S., O'Connor, W. T., Antonelli, T., Rambert, F., & Fuxe, K. (1996a). The vigilance promoting drug modafinil decreases GABA release in the medial preoptic area and in the posterior hypothalamus of the awake rat. Possible involvement of the serotonergic 5-HT₃ receptor. *Neuroscience Letters*, 220, 5-8.
- Ferraro, L., Tanganelli, S., O'Connor, W. T., Antonelli, T., Rambert, F., & Fuxe, K. (1996b). The vigilance promoting drug modafinil increases dopamine release in the rat nucleus accumbens via the involvement of a local gabaergic mechanism. *European Journal of Pharmacology*, 306, 33-39.
- Grether, W. F. (1973). Human performance at elevated environmental temperatures. *Aerospace Medicine*, 44, 747-755.
- Hancock, P. A. (1986). Sustained attention under thermal stress. *Psychological Bulletin*, 99, 263-281.
- Hancock, P. A., & Vasmatazidis, I. (1998). Human occupational and performance limits under stress: The thermal environment as a prototypical example. *Ergonomics*, 41, 1169-1191.
- Hancock, P. A., & Warm, J. S. (1989). A dynamic model of stress and sustained attention. *Human Factors*, 31, 519-537.
- Hockey, G. (1986). Changes in operator efficiency as a function of environmental stress, fatigue, and circadian rhythms. In K. Boff, R. L. Kaufman, & J. P. Thomas (Eds.), *Handbook of perception and human performance*: Vol. 2. *Cognitive processes and performance* (pp. 44-1-44-9). Westport, CT: Greenwood.
- Kahneman, D. (1973). *Attention and effort*. Englewood Cliffs, NJ: Prentice Hall.
- Krueger, G. P. (1989). Sustained work, fatigue, sleep loss and performance: A review of the issues. *Work & Stress*, 3, 129-141.
- Krueger, G. P. (1991). Sustained military performance in continuous operations: Combatant fatigue, rest, and sleep needs. In R. Gal & A. D. Mangelsdorf (Eds.), *Handbook of military psychology* (pp. 255-277). Chichester, England: Wiley.
- Laboratoire L. Lafon. (1994). *Modiodal®*, modafinil: Dossier d'information medical et pharmaceutique (Modiodal®; modafinil: Medical and pharmaceutical information report). Maisons-Alfort, France: Author.
- Laffont, F., Mayer, G., & Minz, M. (1994). Modafinil in diurnal sleepiness: A study of 123 patients. *Sleep*, 17(Suppl. 8), 113-115.

- Lagarde, D., & Batejat, D. (1995). Disrupted sleep-wake rhythm and performance: Advantages of modafinil. *Military Psychology*, 7, 165-191.
- Lia, J., Gervasoni, D., Hou, Y., Vaani-Mercier, G., Rambert, P., Frydman, A., & Jouvet, M. (2000). Effects of amphetamine and modafinil on the sleep/wake cycle during experimental hypersomnia induced by sleep deprivation in the cat. *Journal of Sleep Research*, 9, 89-96.
- Lyons, T., & French, J. (1991). Modafinil: The unique properties of a new stimulant. *Aviation, Space, and Environmental Medicine*, 62, 432-435.
- McLellan, T. M., Ducharme, M., Camin, F., Moroz, D., Bell, D., Baranski, J. V., Gil, V., Buguet, A., & Radomski, M. (2002). *Effect of modafinil on thermoregulation during sleep deprivation and exercise in a warm environment*. Manuscript submitted for publication.
- Mignot, E., Nishino, S., Guilleminault, C., & Dement, W. (1994). Modafinil binds to the dopamine uptake carrier with low affinity. *Sleep*, 17, 436-437.
- Mizuno, K., Asano, K., & Okamoto, K. (1998). Effect of night exercise on the following partially deprived sleep. *Psychiatry and Clinical Neuroscience*, 52, 137-138.
- Murphy, P. J., & Campbell, S. S. (1997). Nighttime drop in body temperature: A physiological trigger for sleep onset? *Sleep*, 20, 505-511.
- Pepler, R. D. (1959). Warmth and lack of sleep: Accuracy or activity reduced. *Journal of Comparative and Physiological Psychology*, 52, 446-450.
- Pigeau, R., Naitoh, P., Buguet, A., McCann, C., Baranski, J., Taylor, M., Thompson, M., & Mack, I. (1995). Modafinil, d-amphetamine, and placebo during 64 hours of sustained mental work: I. Effects on mood, fatigue, cognitive performance, and body temperature. *Journal of Sleep Research*, 4, 212-228.
- Poulton, E. C. (1970). *Environment and human efficiency*. Springfield, IL: Thomas.
- Poulton, E. C., Edwards, R. S., & Colquhoun, W. P. (1974). The interaction of the loss of a night's sleep with mild heat: Task variables. *Ergonomics*, 17, 59-73.
- Ramsey, J. D. (1983). Heat and cold. In G. R. J. Hockey (Ed.), *Stress and fatigue in human performance* (pp. 33-60). Chichester, England: Wiley.
- Ramsey, J. D. (1995). Task performance in heat: A review. *Ergonomics*, 38, 154-165.
- Saletu, B., Frey, R., Krupka, M., Anderer, P., Grunberger, J., & Barbanoj, M. (1999). Differential effects of a new central adrenergic agonist—modafinil—and d-amphetamine on sleep and early morning behaviour in young healthy volunteers. *International Journal of Chemical and Pharmacological Research*, 9, 183-195.
- Warot, D., Corruble, E., Payan, C., Weil, J. S., & Puech, A. J. (1993). Subjective effects of modafinil, a new central adrenergic stimulant in healthy volunteers: A comparison with amphetamine, caffeine, and placebo. *European Journal of Psychiatry*, 8, 201-208.
- Wickens, C. D. (1980). The structure of attentional resources. In R. S. Nickerson & R. Pew (Eds.), *Attention and performance VIII* (pp. 239-257). Hillsdale, NJ: Lawrence Erlbaum Associates, Inc.
- Wing, J. F. (1965). *A review of the effect of high ambient temperature on mental performance* (Tech. Rep. No. AMRL-TR-65-103). Wright-Patterson Air Force Base, OH: Aerospace Medical Research Laboratories.

